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| 09/735,713 | 12/12/2000 | D. Wade Walke | LEX-0108-USA | 5588 |

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| EXAMINER |
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SWOPE, SHERIDAN

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| ART UNIT | PAPER NUMBER |
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1652

DATE MAILED: 07/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/735,713

Applicant(s)

WALKE ET AL.

Examiner

Sheridan L. Swope

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Claims 1-3, directed to nucleic acid molecules encoding proteases, class 536, subclass 23.2, are pending and constitute a single invention. Claims 1-3 are hereby considered.

Specification-Objection

The title of the disclosure is objected to for the use of the word "novel"; all patents are novel. Correction is required.

The abstract of the disclosure is objected to because it does not reflect the subject of the instant application. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Utility

Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Applicants assert that the claimed polynucleotides have utility for microarrays or other assays to screen genetic material from patients; identification of mutations associated with SEQ ID NO: 1; diagnostic assays; preparation of anti-sense oligonucleotides derived from SEQ ID NO: 1; hybridization assays; library screening; analysis of expression patterns; characterization of genomic clones; identification of molecular targets; identification of disease-related mutations; PCR; restriction fragment length polymorphism analysis; isolation of full-length cDNA; preparation of fusion proteins; preparation of antibodies; and as therapeutics. Each of these utilities is an application which would apply to every member of a general class of materials

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and/or is a use only for further research to determine a use for SEQ ID NO: 1 or the protein encoded thereby. As such, these asserted utilities are not specific (for those applicable to all human DNAs) or not substantial because the use of SEQ ID NO: 1 therein is only potential and not in currently available in practical form.

The specification states on page 1 line 33 to page 2 line 2 that the instant protein shares structural similarity to trypsin-like serine proteases, such as oviductin. However, assertion of structural similarity is not an assertion of functional identity or utility. The protein with highest homology to SEQ ID NO: 2 and with known activity, oviductin, shares only 42% identity. While this homology would support the deduction that the protein encoded by SEQ ID NO: 1 is a protease, it is not sufficient to conclude that the instant protein is human oviductin. Said level of identity does not identify the specific substrates or cellular function of the protein encoded by SEQ ID NO: 1. Identification of a substrate for the protease would require further experimentation to identify or confirm a real world use. Thus, neither specific substrates for the instant protein nor specific diseases to be treated with said protein have been identified. Therefore, Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2 is indefinite in the recitation of "hybridizes under stringent conditions" as

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this term is unclear absent a statement of the conditions under which the hybridization reaction is preformed. Nucleic acids that will hybridize under some hybridization conditions, will not necessarily hybridize under different conditions. The hybridization conditions described on page 4 are only exemplary and do not define the conditions recited in Claim 2. Thus, Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim 1 is further rejected under 35 U.S.C. 112, first paragraph. The specification does not provide enablement for any isolated nucleic acid molecule comprising at least 24 contiguous bases of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 1 is so broad as to encompass any polynucleotide sequence comprising at least 24 contiguous bases of SEQ ID NO: 1. The scope of this claim is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claim. Since the amino acid sequence of a protein

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determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO 2 and the nucleotide sequence of SEQ ID NO 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the Claim 1 which, encompasses all polynucleotide sequences that comprising at least 24 contiguous bases of SEQ ID NO: 1. The specification does not support the broad scope of Claim 1 because the specification does not establish: (A) regions of the protein structure encoded by SEQ ID NO: 1 which may be modified without effecting the activity; (B) the general tolerance of said activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides

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insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of proteins with an enormous number of amino acid modifications of the protein encoded by SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules having the limitations of comprising at least 24 continuous bases of SEQ ID NO: 1. The specification does not contain any disclosure of the function of all said nucleic acid sequences. The genus of polynucleotides that comprise these above nucleic acid molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims, including partial sequences. The specification discloses only a single species of the claimed genus which, is insufficient to put one of skill in the art in possession of the attributes and features of all species within the

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claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Yu et al, 1995 or Shibuya et al, 1994. Yu et al teach the sequence of a protein encoded by a polynucleotide having 27 continuous nucleotides that have 100% identity to SEQ ID NO: 1. Shibuya et al teach the sequence of a protein encoded by a polynucleotide having 27 continuous nucleotides that have 100% identity to SEQ ID NO: 1.

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Ashkenazi et al, 2003 (filing date 10-1997) or Wu-Hunter et al, 2001 (filing date 11-1996). Ashkenazi et al teach the sequence of a protein encoded by a polynucleotide having 27 continuous nucleotides that have

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100% identity to SEQ ID NO: 1. Wu-Hunter et al teach the sequence of a protein encoded by a polynucleotide having 24 continuous nucleotides that have 100% identity to SEQ ID NO: 1.

Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Wood et al, 1999. Wood et al teach the sequence of a protein encoded by a polynucleotide having 27 continuous nucleotides that have 100% identity to SEQ ID NO: 1.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan L. Swope, Ph.D.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Delete the word – Novel – from the title.

Replace the abstract with:

Human polynucleotides encoding a protease are disclosed that can be used in therapeutic, diagnostic, and pharmacogenomic applications.

Delete Claim 1.

Replace Claim 2 with:

2. An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof wherein the stringent conditions are hybridization to filter-bound DNA in 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1x SSC/0.1% SDS at 68°C.

Authorization for this examiner's amendment was given in a telephone interview with Lance Ishimoto on June XX, 2003.

Allowable Subject Matter

Claims 2 and 3 are allowed.

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The following is an examiner's statement of reasons for allowance:

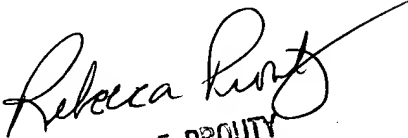
All elected Claims, 2 and 3, are limited to isolated nucleic acid molecules of SEQ ID NO: 1 or encoding the amino acid sequence of SEQ ID NOs: 2. The utility of said polynucleotides, as encoding a serine protease of the trypsin family, is credible based on homology to known proteins; see for example, Yue et al, 2001 (SEQ ID NO: 20; pg 103 Table 3), Hardy et al, 1992 (pg4469, col2, lines1-5 and Fig 7), or Plowman et al, 2002 (SEQ ID NO: 106; parg 0510).

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 8:30-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


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